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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/030,571 | 02/24/1998 | CHARLES R. CANTOR | 25491-2401G | 7542 |

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HELLER EHRMAN WHITE & MCAULIFFE LLP
4350 LA JOLLA VILLAGE DRIVE
7TH FLOOR
SAN DIEGO, CA 92122-1246

| EXAMINER | |
|---|---|
| FORMAN, BETTY J | |
| ART UNIT | PAPER NUMBER |
| 1634 | |

DATE MAILED: 05/27/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/030,571 | CANTOR ET AL. | |
| | Examiner | Art Unit | |
| | BJ Forman | 1634 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *25 April 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *70,72-79,92-94,123,124 and 127-135* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *70,72-79,92-94,123,124 and 127-135* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *April 03* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

## DETAILED ACTION

### *Continued Examination Under 37 CFR 1.114*

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 25 April 2003 has been entered.

2. This action is in response to papers filed 25 April 2003 in which claims 70, 73 and 74 were amended, claims 125-126 were canceled and claims 127-135 were added. All of the amendments have been thoroughly reviewed and entered. The previous objection to the specification and rejection under 35 U.S.C. 112, first and second paragraph are withdrawn in view of the amendments. The previous rejection of Claims 73, 74-76, 92-94 and 123-124 are withdrawn in view of the amendments. The previous rejections of Claims 70, 72, 77-79 are maintained. All of the arguments have been thoroughly reviewed but are deemed moot in view of the amendments to all independent claims. The arguments are addressed as they apply to the instant rejections. New grounds for rejection necessitated by amendment are discussed.

Claims 70, 72-79, 92-24, 123-124 and 127-135 are under prosecution.

### *Specification*

3. The amendment filed 25 April 2003 is objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall

introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows:

Claim 70 has been amended to recite "a degenerate single-stranded portion at the 5' terminus". Applicant cites page 12, lines 1-5 for support for the amendment. The cited passage reads:

> [This variation of the]
> Invention is based on the theory of degenerated probes proposed by S.C. Macevicz (International Patent Application, US 89-04741, published 1989, and herein specifically incorporated by reference). The probes are divided into four subsets. In each, one of the four bases is used at a defined number of positions and all other bases except that one on the remaining positions.

While the passage mentions "degenerated probes" the passage does not teach or provide support for the newly recited "a degenerate single-stranded portion at the 5' terminus".

Claim 74 has been amended to recite "an adjacent sequence of nucleotides comprising ligated nucleic acid present in a target nucleic acid". Applicant cites pages 19, 26, 27, 46 and 47 and Fig. 10 and 11 for support for the amendment. The cited passages are exemplified by the passage on page 27 which recites:

Another embodiment of the invention is directed to a method for creating a nucleic acid probe comprising the steps of (a) synthesizing a plurality of single- stranded first nucleic acids and a set of longer single-stranded second nucleic acids complimentary to the first nucleic acid with a random terminal nucleotide sequence, (b) hybridizing the first nucleic acids to the second nucleic acids to form hybrids having a double-stranded portion and a single-stranded portion with the random nucleotide sequence in the single-stranded portion, (c) hybridizing a single-stranded nucleic acid target to the hybrids, (d) **ligating the hybridized target to the first nucleic acid of the hybrid.**

While the cited passages provide support for ligating hybridized target, the passages do not provide support the newly claimed "adjacent sequence of nucleotides comprising ligated nucleic acid present in a target nucleic acid".

Therefore the amendments to Claims 70 and 74 introduce new matter into the disclosure of the specification.

Applicant is required to cancel the new matter in the reply to this Office Action.

***Claim Rejections - 35 USC § 112***

**35 U.S.C. 112: first paragraph**

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 70, 72-79, 92-94, 123-124 and 134-135 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The recitation "a degenerate single-stranded portion at the 5' terminus" has been added to independent Claim 70 from which Claims 72-73 and 77-79 depend. However, the specification does not provide support for the newly claimed limitation. Applicant cites page 12, lines 1-5 for support for the amendment. The cited passage reads:

> [This variation of the]
> invention is based on the theory of degenerated probes proposed by S.C. Macers (International Patent Application, US 89-04741, published 1989, and herein specifically incorporated by reference). The probes are divided into four subsets. In each, one of

the four bases is used at a defined number of positions and all other bases except that one on the remaining positions.

While the passage mentions "degeneraged probes" the passage does not teach or provide support for the newly claimed "a degenerate single-stranded portion at the 5' terminus".

The recitation "an adjacent sequence of nucleotides comprising ligated nucleic acid present in a target nucleic acid" has been added to independent Claim 74 from which Claims 75-76, 92-24, 123-124 and 134-135 depend. However, the specification does not provide support for the newly added limitation. Applicant cites pages 19, 26, 27, 46 and 47 and Fig. 10 and 11 for support for the amendment. The cited passages are exemplified by the passage on page 27 which recites:

Another embodiment of the invention is directed to a method for creating a nucleic acid probe comprising the steps of (a) synthesizing a plurality of single- stranded first nucleic acids and a set of longer single-stranded second nucleic acids complimentary to the first nucleic acid with a random terminal nucleotide sequence, (b) hybridizing the first nucleic acids to the second nucleic acids to form hybrids having a double-stranded portion and a single-stranded portion with the random nucleotide sequence in the single-stranded portion, (c) hybridizing a single-stranded nucleic acid target to the hybrids, (d) **ligating the hybridized target to the first nucleic acid of the hybrid.**

While the cited passages provide support for ligating hybridized target, the passages do not provide support the newly claimed "adjacent sequence of nucleotides comprising ligated nucleic acid present in a target nucleic acid".

Therefore, the specification fails to define or provide any disclosure to support the newly added limitations of claims 70 and 74.

MPEP 2163.06 notes "IF NEW MATTER IS ADDED TO THE CLAIMS, THE EXAMINER SHOULD REJECT THE CLAIMS UNDER 35 U.S.C. 112, FIRST PARAGRAPH - WRITTEN DESCRIPTION REQUIREMENT. *IN RE RASMUSSEN*, 650 F.2D 1212, 211 USPQ 323 (CCPA 1981)." MPEP 2163.02 teaches that "Whenever the issue arises, the fundamental factual inquiry is whether a claim defines an invention that is clearly conveyed to those skilled in the art at the time the application was filed...If a claim is amended to include subject matter, limitations, or terminology not present in the application as filed, involving a departure from, addition to, or deletion from the disclosure of the application as filed, the examiner should conclude that the claimed subject matter is not described in that application." MPEP 2163.06 further notes "WHEN AN AMENDMENT IS FILED IN REPLY TO AN OBJECTION OR REJECTION BASED ON 35 U.S.C. 112, FIRST PARAGRAPH, A STUDY OF THE ENTIRE APPLICATION IS OFTEN NECESSARY TO DETERMINE WHETHER OR NOT "NEW MATTER" IS INVOLVED. *APPLICANT SHOULD THEREFORE SPECIFICALLY POINT OUT THE SUPPORT FOR ANY AMENDMENTS MADE TO THE DISCLOSURE*" (emphasis added).

**35 U.S.C. 112: second paragraph**

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 74-76, 92-94, 123-124, 127-132 and 134-135 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 74-76, 92-94, 123-124 and 134-135 are indefinite in Claim 74 for the recitation "and an adjacent sequence of nucleotide comprising ligated nucleic acid present in a target nucleic acid" because it is unclear whether the "adjacent sequence" is hybridized to the single-stranded portion or whether the "adjacent sequence" is adjacent to the probe on the array. It is suggested that Claim 74 be amended to clarify as described in the specification.

Claim 127-132 are indefinite in Claim 127, line 6 for the recitation "that base" because it is unclear whether the recitation refers to the "one base" recited in line 5. It is suggested that Claim 127 be amended to clarify e.g. replace "that" with "said one".

Claim 134 is indefinite for the recitation "gapped segment" because it is unclear how "gapped" limits a segment. The specification, page 12 mentions "gapped segment". The passage states:

> In addition it is also a method of the present invention to utilize probes wherein the random nucleotide sequence contains gapped segments, **or** positions along the random sequence which will base pair with any nucleotide or at least not interfere with adjacent base pairing.

However, the passage is unclear regarding whether the gapped segments comprise positions along the random sequence.....or whether the random sequence contains gapped sequences **OR** positions along the random sequence..... Therefore, the specification does not define the instantly claimed gapped segments.

***Claim Rejections - 35 USC § 102***

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the

international application designated the United States and was published under Article 21(2) of such treaty in the English language.

9. Claims 70 and 72 are rejected under 35 U.S.C. 102(e) as being anticipated by Deugau et al (U.S. Patent No. 5,508,169, filed 6 April 1990).

Regarding Claim 70, Deugau et al disclose an array of nucleic acid probes (i.e. complete panel of indexing linkers) wherein each probe has a double-stranded portion at the 3' terminus, a single stranded portion at the 5' terminus and a random nucleotide sequence of length R within the single-stranded portion (Column 11, lines 14-25, Fig. 2 and Claim 33). Figure 2 clearly illustrates the embodiment of Deugau probe comprising a double-stranded portion at the 3' terminus and a single stranded portion at the 5' terminus. As such, Deugau et al clearly disclose the nucleic acid probes of Claim 70. The claim has been amended to recite "a degenerate single-stranded portion". However, it is unclear how the newly claimed degenerate portion differs from the random nucleotide sequence. Furthermore, the specification does not teach and/or clarify a difference. The claims are given the broadest reasonable interpretation consistent with the indefinite claim language and specification wherein the newly claimed degenerate portion is not defined or described.

The courts have stated that claims must be given their broadest reasonable interpretation consistent with the specification *In re Morris*, 127 F.3d 1048, 1054-55, 44 USPQ2d 1023, 1027-28 (Fed. Cir. 1997); *In re Prater*, 415 F.2d 1393, 1404-05, 162 USPQ 541, 550-551 (CCPA 1969); and *In re Zletz*, 893 F.2d 319, 321-22, 13 USPQ2d 1320, 1322 (Fed. Cir. 1989) (see MPEP 2111).

Because Deugau et al disclose the random sequence and because the specification and claims do not define or describe a difference between a random sequence and degenerate portion, Deugau et al disclose the array as claimed.

Regarding Claim 72, Deugau et al disclose the array wherein the double-stranded portion (i.e. common sequence # 1026, # 1504 and # 1701) is between about 3-20 nucleotide

and the single stranded portion is between about 3-20 nucleotides (Columns 15-16, Table I and Table II).

**Response to Arguments**

10. Applicant states that Deugau et al does not teach an array of probes comprising a degenerate single-stranded portion at the 5' end. Applicant cites the specification for a definition of the instantly claimed degenerate probes. However, the instant claims recite " degenerate probe at the 5' terminus. As discussed above, the cited passage does not teach or describe the instantly claimed degenerate probe at the 5' terminus. The passage merely states that the invention "is based on degenerated probes". While the passage provides details on how to design probes, the passage is unclear as to whether the designed probes are degenerate, let alone degenerate at the 5' terminus.

Furthermore, probes designed by the method cited in the passage are not claimed. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

***Claim Rejections - 35 USC § 103***

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having

ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

12. Claim 73 is rejected under 35 U.S.C. 103(a) as being unpatentable over Deugau et al (U.S. Patent No. 5,508,169, filed 6 April 1990) in view of Brenner et al (Proc. Natl. Acad. Sci. USA, 1989, 86: 88902-8906).

Regarding Claim 73, Deugau et al disclose the array of nucleic acid probes (i.e. complete panel of indexing linkers) wherein each probe has a double-stranded portion at the 3' terminus, a single stranded portion at the 5' terminus and a random nucleotide sequence of length R within the single-stranded portion (Column 11, lines 14-25, Fig. 2 and Claim 33) wherein the probes are immobilized to a solid support (Column 11, lines 14-25) but they do not specifically teach the means by which the probes are immobilized. However, biotin/streptavidin immobilization was well known in the art at the time the claimed invention was made as taught by Brenner et al who teach that biotin/streptavidin provides a versatile means of capture immobilization (page 8904, second full paragraph). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the biotin/streptavidin of Brenner et al to the immobilization of Deugau et al based on the teaching of Brenner et al to thereby provide versatile capture immobilization (page 8904, second full paragraph).

13. Claims 74-79, 92-94, 124, 127, 129-135 are rejected under 35 U.S.C. 103(a) as being unpatentable over Deugau et al (U.S. Patent No. 5,508,169, filed 6 April 1990) in view of Ghosh et al (Nucleic Acids Research, 1987, 15: 5353-5372).

Regarding Claim 74, Deugau et al teach an array of nucleic acid probes wherein each probe comprises a single-stranded portion at one terminus and a double-stranded portion at the opposite terminus wherein the single-stranded portion includes a random nucleotide sequence of length R and one strand of the double-stranded portion is conjugated to a solid support using the method of Ghosh et al (Column 10, lines 45-51, Fig. 2 and Claim 26) but Deugau et al do not specifically teach the probe is conjugated to a coupling agent through which the probes are bound to the solid support. However, Ghosh et al teach the method of binding probes to a solid support wherein the probe is conjugated to a coupling agent (i.e. aminohexyl and cystaminyl functional groups) through which the probes are bound to the solid support (page 5358, second full paragraph). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the coupling agent for probe attachments taught by Ghosh et al to the probe attachments of Deugau et al based on the teaching of Deugau et al wherein their probes are attached using the methods of Ghosh et al for the obvious benefits of utilizing a preferred and successful method of probe attachment as taught by Deugau et al (Column 10, lines 45-51).

Furthermore, Deugau et teach the array wherein the single-stranded portion is hybridized to and ligated to nucleic acids in a target (Column 11,lines 14-15 and Fig. 2).

Regarding Claim 75, Deugau et al teach an array of nucleic acid probes wherein each probe has a double-stranded portion and a single stranded portion and a random nucleotide sequence of length R within the single-stranded portion (Column 9, lines 29-42 and Claim 33) wherein the probes are fixed to a solid support as taught by Ghosh et al (Column 10, lines 45-51 and Claim 26) but they do not specifically teach the material from which the solid support is made. However, Ghosh et al teach their solid support is selected from plastics and resins (page 5356, first full paragraph-page 5357, last paragraph). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the solid supports of Ghosh et al to the immobilization of Deugau et al and to immobilize the probes

onto plastic or resin support based on the suggestion of Deugau et al (Column 10, lines 45-51 and Claim 26) thereby utilizing well known supports for the expected benefits of successful immobilization.

Regarding Claim 76, Deugau et al teach the array wherein the solid support is a two-dimensional matrix with multiple probe binding sites i.e. the probes are attached to spatially segregated solid phase substrates (Column 10, lines 45-51).

Regarding Claim 77, Deugau et al teach the array wherein the probes are labeled with a detectable label (Claim 27).

Regarding Claim 78, Deugau et al teach the array wherein the label comprises a radioisotope or fluorescent chemical (Claims 27 & 28).

Regarding Claim 79, Deugau et al teach the array wherein the nucleic acids are DNA (Claims 25 and 33).

Regarding Claim 92, Deugau et al teach the array wherein the probes are labeled with a detectable label (Claim 27).

Regarding Claim 93, Deugau et al teach the array wherein the label comprises a radioisotope or fluorescent chemical (Claims 27 & 28).

Regarding Claim 94, Deugau et al teach the array wherein the nucleic acids are DNA (Claims 25 and 33).

Regarding Claim 124, Deugau et al teach the array comprising about $4^r$ different nucleic acid probes (i.e. complete panel of indexing linkers) (Column 11,lines 14-25).

Regarding Claim 127, Deugau et al teach an array of nucleic acid probes (i.e. complete panel of indexing linkers) wherein each probe has a double-stranded portion at the 3' terminus, a single stranded portion at the 5' terminus and a random nucleotide sequence of length R within the single-stranded portion (Column 11, lines 14-25, Fig. 2 and Claim 33). Figure 2 clearly illustrates the embodiment of Deugau probe comprising a double-stranded portion at the 3' terminus and a single stranded portion at the 5' terminus. but Deugau et al do not

specifically teach the probe is conjugated to a coupling agent through which the probes are bound to the solid support. However, Ghosh et al teach the method of binding probes to a solid support wherein the probe is conjugated to a coupling agent (i.e. aminohexyl and cystaminyl functional groups) through which the probes are bound to the solid support (page 5358, second full paragraph). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the coupling agent for probe attachments taught by Ghosh et al to the probe attachments of Deugau et al based on the teaching of Deugau et al wherein their probes are attached using the methods of Ghosh et al for the obvious benefits of utilizing a preferred and successful method of probe attachment as taught by Deugau et al (Column 10, lines 45-51).

The claim recites "within the single-stranded portion of each probe, one base is used at a defined number of positions and all bases except that base are in the remaining positions". Deugau et al teach their single-stranded portions are selected from all possible permutations and combinations of A, C, G, T (Column 9, lines 16-27). The single-stranded portions of Deugau et al inherently have one base and X number of positions and the other bases would be in the remaining positions. The claim appears to be reciting a method step or mental step for defining or designing the single-stranded portions of the probe. However, the claim is drawn to a produce i.e. array comprising nucleic acid probes. The courts have stated that "even though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985) see MPEP 2113.

Regarding Claim 129, Deugau et al teach the array wherein the probes are labeled with a detectable label (Claim 27).

Regarding Claim 130, Deugau et al teach the array wherein the label comprises a radioisotope or fluorescent chemical (Claims 27 & 28).

Regarding Claim 131, Deugau et al teach the array wherein the nucleic acids are DNA (Claims 25 and 33).

Regarding Claim 132, Deugau et al teach an array of nucleic acid probes wherein each probe has a double-stranded portion and a single stranded portion and a random nucleotide sequence of length R within the single-stranded portion (Column 9, lines 29-42 and Claim 33) wherein the probes are fixed to a solid support as taught by Ghosh et al (Column 10, lines 45-51 and Claim 26) but they do not specifically teach the material from which the solid support is made. However, Ghosh et al teach their solid support is selected from plastics and resins (page 5356, first full paragraph-page 5357, last paragraph). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the solid supports of Ghosh et al to the immobilization of Deugau et al and to immobilize the probes onto plastic or resin support based on the suggestion of Deugau et al (Column 10, lines 45-51 and Claim 26) thereby utilizing well known supports for the expected benefits of successful immobilization.

Regarding Claim 133, Deugau et al teach the support is two dimensional i.e. an array wherein each member of the array is attached to spatially separate part of a support (Column 11, lines 23-25).

Regarding Claim 134, Deugau et al teach the support wherein the random sequence includes a gapped segment i.e. prior to ligation of the DNA fragment, there is a gap at the end of the random sequence (Column 11, lines 14-15 and Fig. 2).

The claims are given the broadest reasonable interpretation consistent with the indefinite claim language and specification wherein "gapped segment" is not described or defined. The courts have stated that claims must be given their broadest reasonable interpretation consistent with the specification *In re Morris*, 127 F.3d 1048, 1054-55,

44 USPQ2d 1023, 1027-28 (Fed. Cir. 1997); *In re Prater*, 415 F.2d 1393, 1404-05, 162 USPQ 541, 550-551 (CCPA 1969); and *In re Zletz*, 893 F.2d 319, 321-22, 13 USPQ2d 1320, 1322 (Fed. Cir. 1989) (see MPEP 2111). Given the broadest reasonable interpretation, the gap at the end of the random sequence is encompassed by the instantly claimed "gapped segment".

Regarding Claim 135, Deugau et al teach the array wherein the nucleic acid comprises at least one modified base i.e. labeled with a reporter group (Column 11, lines 17-20).

**Response to Arguments**

14. Applicant argues that Deugau et at. does not teach or suggest an indexing linker having a single-stranded portion that includes a random nucleotide sequence that includes a nucleotide sequence comprising ligated nucleic acid present in a target nucleic acid. The argument has been considered but is not found persuasive because as stated above, Deugau et al teach the ligated sequence as claimed.

16. Claim 123 and 128 are rejected under 35 U.S.C. 103(a) as being unpatentable over Deugau et al (U.S. Patent No. 5,508,169, filed 6 April 1990) and Ghosh et al (Nucleic Acids Research, 1987, 15: 5353-5372) as applied to Claim 74 above and further in view of Brenner et al (Proc. Natl. Acad. Sci. USA, 1989, 86: 8902-8906).

Regarding Claims 123 and 128, Deugau et al teach an array of nucleic acid probes wherein each probe comprises a single-stranded portion at one terminus and a double-

stranded portion at the opposite terminus wherein the single-stranded portion includes a random nucleotide sequence of length R and one strand of the double-stranded portion is conjugated to a solid support using the method of Ghosh et al (Column 10, lines 45-51, Fig. 2 and Claim 26) and Ghosh et al teach the method of binding probes to a solid support wherein the probe is conjugated to a coupling agent (i.e. aminohexyl and cystaminyl functional groups) through which the probes are bound to the solid support (page 5358, second full paragraph). Deugau et al and Ghosh et al do not teach a coupling agent selected from the group consisting of antibody/antigen, biotin/streptavidin, *Staphylococcus aureus* protein A/IgG antibody $F_c$ fragment, nucleic acid/nucleic acid binding protein, and streptavidin/protein A chimeras. However, biotin/streptavidin coupling agents were well known in the art at the time the claimed invention was made as taught by Brenner et al who teach biotin/streptavidin is a preferred coupling agent wherein the biotin coupling agent can be attached to either the 3' or 5' end and facilitates enhancement of sequence fingerprinting via selective immobilization (page 8904, second full paragraph). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the biotin/streptavidin coupling agent of Brenner et al to the Deugau et al array of probes to thereby selectively immobilize probes for fingerprinting as taught by Brenner (page 8904, second full paragraph) for the obvious benefits of providing an array of selectively immobilized probe e.g. providing means for selective hybridization.

**Response to Arguments**

Applicant reiterates the arguments above regarding each probe including a single-stranded portion including a random nucleotide sequence of length R and an adjacent nucleotide sequence including ligated nucleic acid present in a target nucleic acid and further argues that Brenner et at. does not cure this defect. The argument has been considered but is not found persuasive because a stated above, Deugau et al teach the ligated sequence as claimed.

**Conclusion**

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to BJ Forman whose telephone number is (703) 306-5878. The examiner can normally be reached on 6:30 TO 4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones can be reached on (703) 308-1152. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-8724 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

BJ Forman, Ph.D.
Patent Examiner
Art Unit: 1634
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